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ORIGINAL RESEARCH

Analysis of clinical and biochemical parameters to differentiate between antepartum and intrapartum asphyxia

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ABSTRACT

Background: Perinatal asphyxia is a clinical or biochemical evidence of lack of oxygen or excess of carbon dioxide in the body, due to failure of efficient respiration at birth with resultant hypoxia and acidemia. It is also of medicolegal importance to know the exact cause of fetal distress whether it is antepartum or intrapartum. This study was undertaken to evaluate the use of cord blood serum erythropoietin (S. Epo) and blood gas analysis as a predictor to differentiate between antepartum and intrapartum asphyxia.

Material and Methods: A prospective cross- sectional study on 60 neonates born at term in the labor room of a tertiary hospital setting. Through clinical history and examination, cord blood serum erythropoietin and arterial blood gas analysis was performed in each case. Mild to moderate hypoxic-ischaemic encephalopathy (HIE) cases were treated with 500U/kg of recombinant human erythropoietin every alternate day for two weeks, with the first dose administered by 48 hours of life.

Results: Out of the 60 neonates, 68.3% required treatment with rHuEPO, Only those affordable of the treatment, (26.7%) were given rHuEPO. Amongst the 41 neonates with elevated S.Epo, 53.7% weighed<2.5 kg (mean weight- 2.52 kg). Low APGAR Score at 1 min (in 71.7% neonates) and 5 min (in 93.3% neonates) were strongly associated with increased levels of erythropoietin (p≤0.00). Cord blood pH showed acidosis in majority (71.7%) of the cases, while 28.3% had normal cord blood pH.

Conclusion: High levels of S.Epo is associated with antepartum asphyxia while normal S.Epo level with low pH is associated with an intrapartum cause of asphyxia.

Keywords: Perinatal asphyxia, Cord blood erythropoietin, Recombinant human erythropoietin

INTRODUCTION

Perinatal asphyxia remains a significant cause of perinatal morbidity & mortality all over the world.[1] Various incidences of cerebral palsy and mental retardation have been reported with low risk women having an uneventful antenatal period. The obstetrician is responsible for the early detection of a hypoxic event in order to prevent a neurological deficit.[2] The fetus reacts to hypoxemia by extracting more oxygen from the blood and this period is associated with reduced fetal movements and the absence of fetal heart rate (FHR) accelerations.[3]With hypoxia, there is a catecholamine surge causing vasoconstriction in non-essential organs (skin, muscle, bone, liver, intestines, and kidneys), and an increase in cardiac output by

raising the heart rate. It is also of medicolegal importance to know the exact cause of fetal distress whether it is antepartum or intrapartum.[3]
Mechanisms of perinatal asphyxia have been described:
1. Interruption of umbilical circulation (Cord compression/accidents) 2. Inadequate perfusion of maternal side of placenta (maternal hypotension/ hypertension/ abnormal uterine contractions). 3. Altered placental gas exchange (abruption placentae/placenta previa/ placental insufficiency). 4. Impaired maternal oxygenation (cardiopulmonary disease/anemia). 5. Failure of the neonate to accomplish lung inflation and transition from fetal to neonatal cardiopulmonary circulation.[4]
Erythropoietin (Epo) is a glycoprotein that is produced mainly by interstitial fibroblasts in the kidneys of the adult and in hepatocytes in the fetus. Under normal conditions, Epo production is mediated by hypoxemia. Thus, cord blood serum erythropoietin (S.Epo) gives us a clear picture of the underlying hypoxia. Recently, Epo has emerged as a multifunctional growth factor that plays an important role in the nervous system as a potent neuroprotector.[5]
Recombinant human erythropoietin (rHuEPO) has been found to prevent neuronal injury in neonates, especially under conditions of chronically reduced blood flow (chronic ischaemia).
Umbilical arterial acidemia forms an objective biochemical hallmark of asphyxia. The mode of delivery and duration of the second stage of laborinfluence cord blood gas analysis; as does the time of collection and method of sample storage.[6] Cord blood serum erythropoietin (S.Epo) gives us a clear picture of the underlying hypoxia.[7]This study was undertaken to evaluate the use of cord blood serum erythropoietin (S. Epo) and blood gas analysis as a predictor to differentiate between antepartum and intrapartum asphyxia.

AIM & OBJECTIVES

The aim of the study is to evaluate the use of cord blood S.Epo and blood gas analysis as a predictor to differentiate between antepartum and intrapartum asphyxia.It also led to improvement in neuro developmental outcomes in asphyxiated neonates who were treated immediately with recombinant human erythropoietin (rHuEPO).

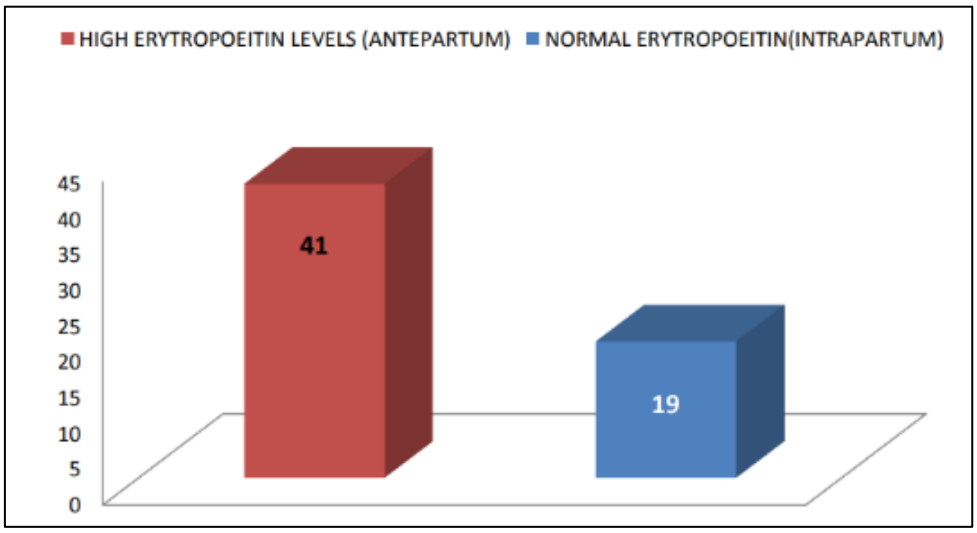
MATERIAL AND METHOD

A cross-sectional prospectivestudy of sixty neonates cases born at term in labor room of a tertiary hospital to pregnant women in a period of two years.
Inclusion Criteria: Uncomplicated term pregnancies delivering vaginally and pregnant women delivering by caesarean section with fetal outcome showing low apgar score.
Exclusion Criteria: Preganancy induced hypertension, gestational diabetes mellitus and Rh – immunized pregnancies.
Following informed consent, thorough clinical history and examination, cord blood serum erythropoietin and arterial blood gas analysis was performed in each case. Mild to moderate hypoxic-ischaemic encephalopathy (HIE) cases were treated with 500U/kg of recombinant human erythropoietin every alternate day for two weeks, with the first dose administered by 48 hours of life. The results were statistically analysed.

RESULTS

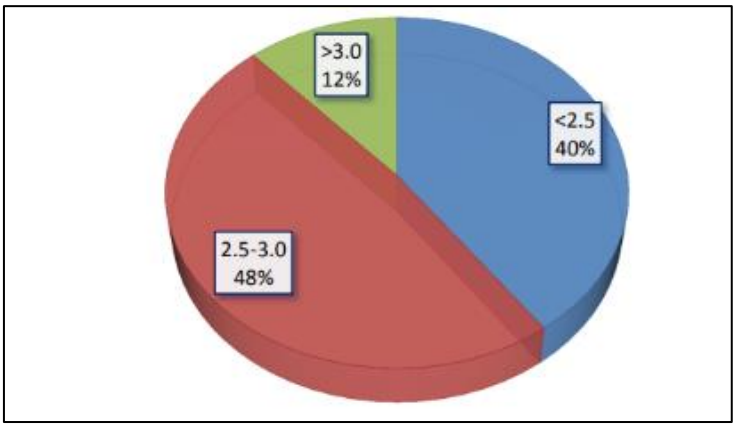
Of the 60 cases, majority (68.3%) had a high S.Epo level suggesting it to be an antepartum asphyxic event whereas the others (31.7%) with a normalS. Epo level indicating an intrapartum asphyxic event ($p \leq 0.02$) as shown in figure 1.

Figure1: relation of antepartum and intrapartum asphyxia to high versus normal erythropoietin levels



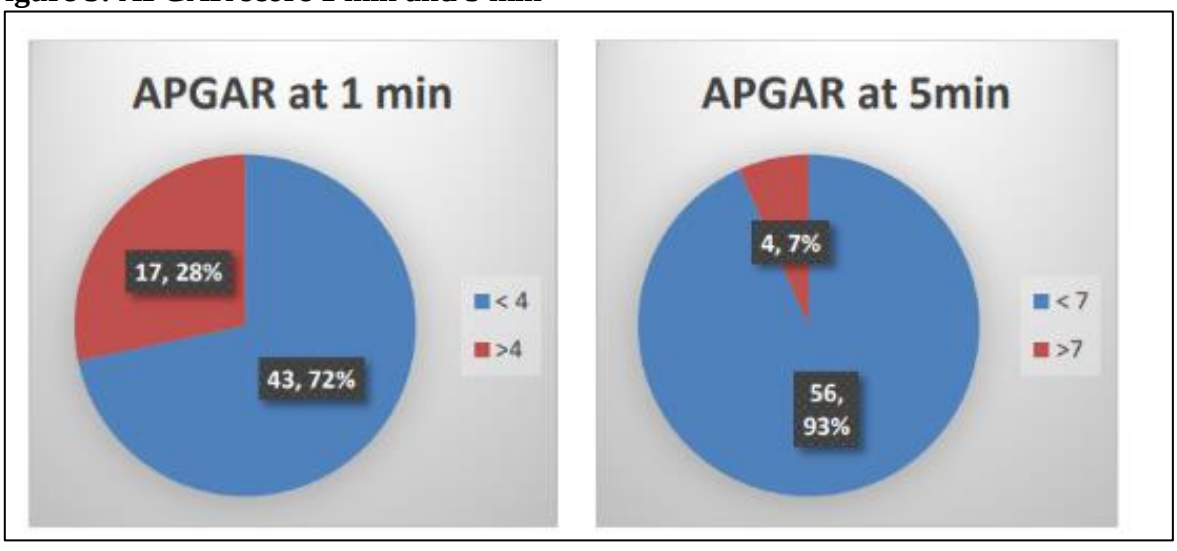
Amongst the 41 neonates with elevated S.Epo, 53.7% weighed<2.5 kg (mean weight- 2.52 kg) as shown in figure 2.

Figure 2: Weight in neonates



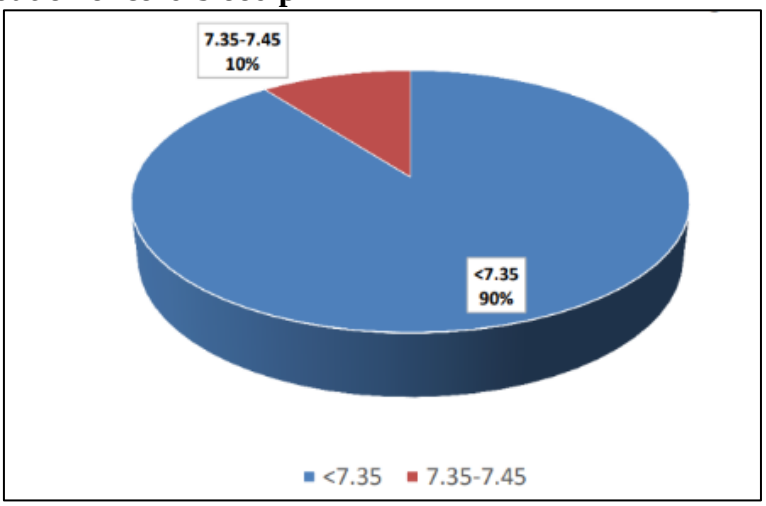
Low APGAR Score at 1 min (in 71.7% neonates) and 5 min (in 93.3% neonates) were strongly associated withincreased levels of erythropoietin (p≤0.00) as shown in figure 3.

Figure 3: APGAR score 1 min and 5 min



Cord blood pH showed acidosis in majority (71.7%) of the cases, while 28.3% had normal cord blood pH. Of the 41 patients whose S. Epo levels were high, 58.5% had a pH <7.35 and 41.5% had a normal pH as given in Figure 4.

Figure 4: Distribution of cord blood pH



Amongst the asphyxiated neonates only 63% of them required neonatal intensive care unit (NICU) admission as shown in Figure 5. Out of the 60 neonates, 68.3% required treatment with rHuEPO, Only those affordable of the treatment, (26.7%) were givenrHuEPO as given in figure 6.

Figure 5: NICU admission

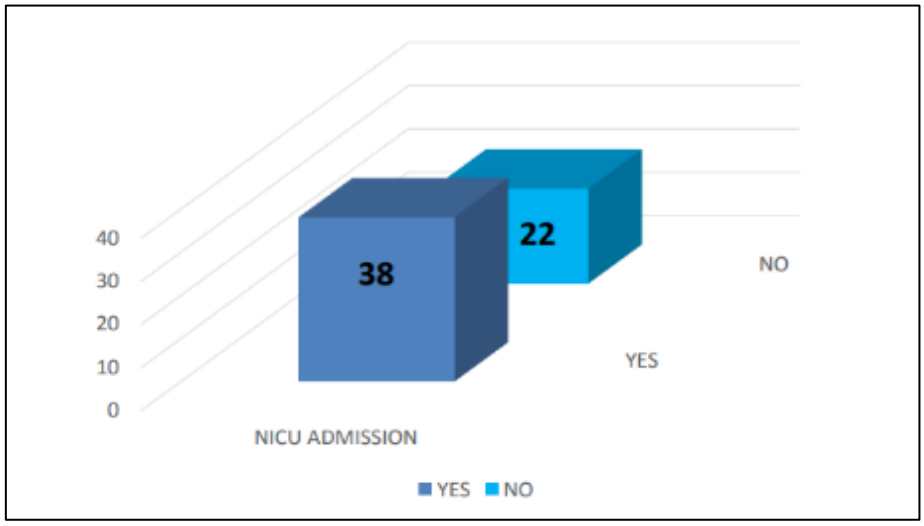
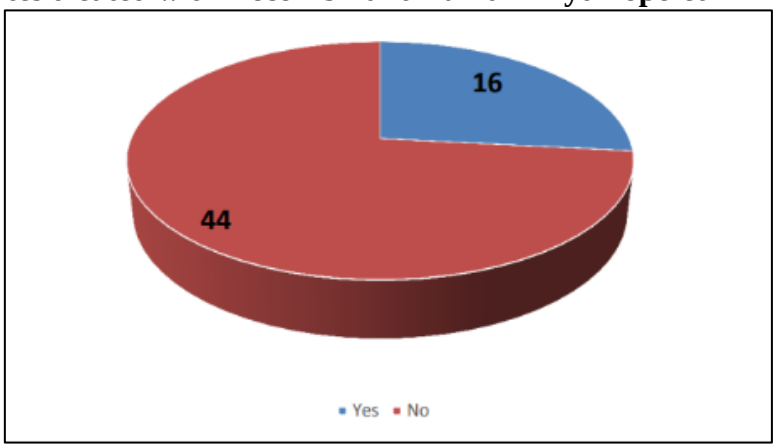


Figure 6: Neonates treated with Recombinant Human Erythropoietin



They were found to require lesser ventilatory support, shorter NICU care, earlier weaning off of oxygen and lesser dose of antiepileptics at the time of discharge.

DISCUSSION

In the present study, cord blood S.Epo and blood gas analysis were evaluated to differentiate between antepartum and intrapartum asphyxia. We also administered rHuEPO to improve neurodevelopment outcomes in neonates with chronic asphyxia.

Ruth et al and Widness et al, found higher levels of S.Epo in infants born spontaneously after labor compared to those delivered by primary LSCS before labor. This led them to conclude that fetuses experiencing labor maybe exposed to a greater degree of intrauterine hypoxia. Our findings were in concordance with those of these studies.[8,9]

In the present study, majority (33.3%) were electively taken for LSCS in view of not willing for vaginal birth after caesarean section while the other indications were caesarean done at maternal request (14.8%), previous two LSCS (14.8%), previous LSCS with breech presentation (14.8%), transverse lie (14.8%) and primigravida with breech presentation (7.4%).

Ruth et al and Maier et al found a correlation between cord blood erythropoietin levels and the degree of fetal growth retardation. They found increased S. Epo levels in SGA infants suggesting a prolonged period of hypoxia. [8,10]

However, Eckardt et al.[11] did not observe any difference in S. Epo levels between adequate for gestational age (AGA) and SGA term infants in the absence of fetal distress. The findings in our study were in accordance with those of Ruth et al and Maier et al.

In our study, low Apgar Score at 1 min and 5 min were highly significant with increased levels of Epo. ($p<0.00$).

In this study, majority (58.5%) of the patients with high S.Epo had clear amniotic fluid and 41.5% showed meconium stained amniotic fluid (MSAF). Richey et al , in their study, concluded that S.Epo. levels were significantly elevated in newborns with MSAF. In our study, however, the levels of S.Epo did not statistically correlate with the number of patients with MSAF. This can be explained by the fact that majority of the patients (33.3%) included in this study underwent elective LSCS.[12-14]

In our study, a mean pO2 of 20.7 mmHg a was observed, with a range of 12.4- 32.2 mm of Hg. We observed that pO2 was found to be reduced in all neonates irrespective of the S.Epo levels. This is in agreement with the observations of Teramo et al and Mair et al.These authors explained that tissue oxygenation depends not only on arterial pO2 but also on the oxygen dissociation, which is influenced by acidosis. Furthermore, fluctuations in arterial pO2 occur more rapidly than those in S.Epo concentration.[15-17]

In the present study, amongst the asphyxiated neonates, 63% of them required NICU admission whereas 37% of them were shifted to mother side with initial resuscitative measures. Majority (89.5%) of cases with normal S.Epo levels did not require NICU admission whereas only 10.5% of them required NICU admission. Of those with increased S.Epo, 87.8% of neonates were admitted in the NICU, while the rest 12.2% neonates did not require NICU admission. The fetus has a period of protection from a partial asphyxic insult because there are cardiovascular compensatory mechanisms leading to increased cerebral blood flow. The significance of asphyxia to the fetus requires not only a measure of degree of the insult but also the duration of asphyxia, as well as compensation of the fetus to the asphyxic insult. Hence, neonates with chronic hypoxia would require post resuscitation care.[18]

CONCLUSION

High levels of S.Epo is associated with antepartum asphyxia while normal S.Epo level with low pH is associated with an intrapartum cause of asphyxia. These markers could serve as evidence in medico-legal situations. The administration of rHuEPO can improve the neurodevelopmental outcomes in mild to moderate HIE neonates.

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